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**REMARKS**

Claims 89-100, 109-128, 137-160 and 169-190 were under examination as of the issuance of the Office Action of October 16, 2003. Claims 89-100, 109-128, 137, 140-145, 148-160 and 169-190 are rejected. Claims 138, 139, 146 and 147 are objected to as dependent upon a rejected base claim.

Claims 140, 148-160, and 169-178 have been canceled. Claims 187-190 have been amended. Specifically, Claim 187 has been amended to correct a grammatical error. Support for this amendment can be found in Example 6 on page 26 (line 21) of the originally filed application. Specifically, claims 188-190 have been amended to correct dependencies in light of the cancellation of claims 149 and 172.

The foregoing amendments and cancellations should in no way be construed as an acquiescence to any of the Examiner's rejections and have been made solely to expedite examination of the present application. No new matter has been added. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s). After entry of these amendments, claims 89-100, 109-128, 137-139, 141-147, and 179-190 are pending in this application.

**Rejection Under 35 U.S.C. § 112, First Paragraph**

In the Office Action of October 16, 2003, the prior rejection of claims 89-100, 109-116 and 179-187 under 35 U.S.C. § 112, first paragraph, as lacking enablement for the full scope of the claims is withdrawn. The Office Action acknowledges that the claims are properly enabled.

Claims 140, 148-160, 169-178 and 188-190 stand rejected under 35 U.S.C. § 112, first paragraph. In order to expedite examination, claims 140, 148-160, and 169-178 are cancelled without prejudice, and claims 188-190 have been amended to depend only from claims directed to *in vitro* applications. Applicants reserve the right to pursue the subject matter of the claims as originally filed in one or more subsequent applications.

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In view of the amendment to the claims, Applicants assert that rejection of claims 140, 148-160, and 169-178 is moot and Applicants further request withdrawal of the rejection of claims 188-190 under 35 U.S.C. § 112, first paragraph.

**Rejection Under 35 U.S.C. § 103**

The Office Action rejects claims 89-100, 109, 111-115, 117-128, 137, 140-145, 148-160, 169, 172-176 and 179-190 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,342,390 to Wiener *et al.* (Wiener) in view of International Patent Publication WO 96/25942 to Mannino and Gould-Fogerite (Mannino).

The outstanding rejection appears to be based on the premise that Mannino teaches cochleates used to transfer DNA and proteins into cells, and that since both Mannino and the primary reference contemplated gene therapy methods, that it would have been obvious to modify Wiener to include the cochleate structure of Mannino. The Office Action reasons that the advantages of cochleates as vehicles for delivery of biologically active molecules taught in Mannino "provides strong motivation to combine the teachings," and that the skilled artisan would have a reasonable expectation of success "in view of the versatility of cochleates as vehicles for transfer of molecules into cells taught" in Mannino.

In a response dated May 5, 2003, Applicants asserted that, in light of the significant differences between cochleates and liposomes, a skilled artisan would not have a reasonable expectation of success to combine the teachings of Wiener and Mannino. The subsequent Office Action of October 16, 2003 states that Mannino teaches that cochleates can deliver nucleic acids into cells and, accordingly, a skilled artisan would have a reasonable expectation of success. The Office Action further cautions that Applicants' assertion that it was unknown whether the claimed combination would be successful "directly contradicts Applicants' own statements made in Mannino *et al.*".

Applicants respectfully disagree. The challenge of the invention disclosed in the pending application is the use of a cochleate to deliver a vector delivery system including one or more proteins and a polynucleotide recognized and bound by the one or more proteins. Applicants agree that Mannino does, in fact, teach that cochleates can successfully deliver nucleic acids. Furthermore, Applicants acknowledge that Mannino teaches that cochleates can successfully deliver polypeptides. However, Mannino does

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not teach or suggest a vector delivery structure as presently claimed. More specifically, Mannino does not teach or suggest a vector delivery system (including an integrative DNA vector recognized and bound to proteins to facilitate integration) in a manner that will allow for integration of the DNA into the host DNA.

In addition, Applicants respectfully reassert their contention that liposomes and cochleates are markedly different. Liposomes and cochleates have different structures, properties and delivery mechanisms. In particular, cochleates provide a vastly different environment for biological molecules to be delivered. For example, a skilled artisan did not necessarily have a reasonable expectation of success that a vector delivery system could be incorporated within the minimal space available between lipid bilayers of a cochleate, a challenge not presented by the use of liposomes which have vast space available within their interior. Moreover, a skilled artisan did not necessarily have a reasonable expectation of success that the vector delivery system could be properly incorporated into the cochleate in a form conducive to ultimately allow for the integration of the DNA within the host DNA, *i.e.*, to allow for the delivery of an intact and active vector delivery system. For example, a skilled artisan may have expected that the integrating proteins would be forced to assume a conformation within the minimal space available in the cochleate that would inactivate the protein, undermine its ability to integrate the DNA within the host DNA, and/or separate the protein from the polynucleotide to which it is bound. Furthermore, a skilled artisan may not have necessarily expected that the vector delivery system could be delivered intact and in an active form when carried in the substantially water free cochleate as opposed to in the less confined structures disclosed in Wiener.

Each of the pending composition or method of use claims recite, directly or indirectly, a nonobvious encochleated vector delivery system including one or more proteins and a polynucleotide recognized and bound by the one or more proteins. Accordingly, Applicants respectfully request withdrawal of the rejection of the pending claims under 35 U.S.C. § 103.

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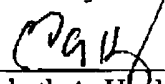
**CONCLUSION**

In view of the foregoing remarks, reconsideration of the rejections and allowance of all pending claims is respectfully requested. If there are any remaining issues or if the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

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